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ELI LILLY AND COMPANY TO PAY U.S. $36 MILLION RELATING TO OFF-LABEL PROMOTION

WASHINGTON, D.C. – American pharmaceutical manufacturer Eli Lilly and Company agreed to plead guilty and to pay $36 million in connection with its illegal promotion of its pharmaceutical drug Evista, the Justice Department announced today.

In pleading guilty to a criminal count of violating the Food, Drug, and Cosmetic Act by misbranding its drug Evista, the Indianapolis-based company agreed to pay a $6 million criminal fine and forfeit to the United States an additional sum of $6 million. In addition to the criminal plea, Lilly has agreed to settle civil Food, Drug, and Cosmetic Act liabilities by entering into a consent decree of permanent injunction and paying the United States $24 million in equitable disgorgement.

Lilly was charged in a criminal information filed today with violation of the Food, Drug, and Cosmetic Act, following an investigation by the Food and Drug Administration's (FDA) Office of Criminal Investigations. A plea agreement signed by Lilly and the United States, a complaint for permanent injunction, and a consent decree of permanent injunction signed by the pharmaceutical company and the United States were also filed with the U.S. District Court for the Southern District of Indiana in Indianapolis.

Evista is approved by the FDA for the prevention and treatment of osteoporosis in post-menopausal women. As alleged in the information, under the provisions of the Food, Drug, and Cosmetic Act, a company must specify in its new drug application to the FDA labeling for all proposed intended uses for the drug. Once approved by the FDA, the drug may not be legally marketed or promoted for so-called "off-label" uses - any use not specified in an application and approved by the FDA.

The information alleges that the first year's sales of Evista in the U.S. were disappointing compared to Lilly's original forecast. According to the information, in October of 1998, the company reduced the forecast of Evista's first year's sales in the U.S. from $401 million to $120

million. An internal Lilly business plan noted that "Disappointing year versus original forecast." The information alleges that in order to expand sales of the drug, Lilly sought to broaden the market for Evista by promoting it for unapproved uses.

The information alleges that Lilly's strategic marketing plans and promotion touted Evista as effective in preventing and reducing the risk of diseases for which the drug's labeling lacked adequate directions for use. According to the information, Lilly's Evista brand team and sales representatives promoted Evista for the prevention and reduction in risk of breast cancer, and the reduction in the risk of cardiovascular disease. Under the provisions of the Food, Drug, and Cosmetic Act, Evista was misbranded when its labeling did not bear adequate directions for each of these intended uses. As alleged in the information, Lilly promoted Evista as effective for reducing the risk of breast cancer, even after Lilly's proposed labeling for this use was specifically rejected by the FDA.

"The Department of Justice is committed to prosecuting the illegal marketing of pharmaceutical drugs," said Robert D. McCallum, Jr., Associate Attorney General. "Promotion by a pharmaceutical company of unapproved uses of a product challenges the drug approval process which has served the country well."

Potential problems that can arise from off-label use without the benefit of careful FDA oversight include the possibility that the promoted drug was used instead of another drug that had already been approved by the FDA for a particular use.

The information alleges that Lilly executed its illegal conduct using a number of tactics, including:

- One-on-one sales pitches by sales representatives promoting Evista to physicians about off-label uses of Evista. Sales representatives were trained to prompt or bait questions by doctors in order to promote Evista for unapproved uses;
- Encouraging sales representatives promoting Evista to send unsolicited medical letters to promote the drug for an unapproved use to doctors on their sales routes;
- Organizing a "market research summit" during which Evista was discussed with physicians for unapproved uses, including reducing the risk of breast cancer; and
- Creating and distributing to sales representatives an "Evista Best Practices" videotape, in which a sales representative states that "Evista truly is the best drug for the prevention of all these diseases" referring to osteoporosis, breast cancer, and cardiovascular disease.

The complaint for permanent injunction alleges that Lilly executed its illegal conduct using a number of additional tactics, including:

- Training sales representatives to promote Evista for the prevention and reduction in the risk of breast cancer by use of a medical reprint in a way that highlighted key results of Evista and thereby promoted Evista to doctors for an unapproved use. Some sales representatives were instructed to hide the disclosure page of the reprint which noted, among other things, that "All of the authors were either employees or paid consultants of Eli Lilly at the time this article was written," and "The prescribing information provides that 'The effectiveness of [Evista] in reducing the risk of breast cancer has not yet been established.'";
- Organizing "consultant meetings" for physicians who prescribed Evista during which unapproved uses of Evista were discussed; and
- Calculating the incremental new prescriptions for doctors who attended Evista advisory board meetings in 1998. The advisory board meetings included discussion of unapproved uses for Evista. By measuring and analyzing incremental new prescriptions for doctors who attended the advisory board meetings, Lilly was using this intervention as a tool to promote and sell Evista.

"Today's action is a result of the close cooperation between the FDA Office of Criminal Investigations and the Department of Justice in investigating this serious matter and seeking appropriate sanctions for it," said Acting FDA Commissioner Dr. Andrew C. von Eschenbach. "These fines and the permanent injunction demonstrate that there is a strong system in place for ensuring that pharmaceutical companies fully comply with all aspects of the drug approval process."

In addition to agreeing to plead guilty to the criminal information and the plea agreement signed by Lilly, the company's settlement with the United States includes the following components:

(a) Lilly has agreed to settle civil Food, Drug, and Cosmetic Act liabilities by entering into a consent decree of permanent injunction and paying the United States $24 million in equitable disgorgement. As part of the consent decree, Lilly has agreed to comply with the terms of a permanent injunction, which will require the company to implement effective training and supervision of its marketing and sales staff for Evista, and ensure that any future off-label marketing conduct is detected and corrected. Lilly has agreed to be permanently enjoined from

directly or indirectly promoting Evista for use in preventing or reducing the risk of breast cancer, reducing the risk of cardiovascular disease, or for any other unapproved use in a manner that violates the Food, Drug, and Cosmetic Act unless and until FDA approves the drug for an additional use or uses.

(b) Also as part of the consent decree, Lilly has agreed to hire and utilize an independent organization to conduct reviews to assist Lilly in assessing and evaluating Lilly's systems, processes, policies, and procedures relating to the promotion of Evista and the company's compliance with the consent decree.

The FDA made the following announcement to postmenopausal women who have taken Evista for the prevention or treatment of osteoporosis: “No postmenopausal woman who has taken Evista for the prevention or treatment of osteoporosis is affected by this action, as this matter today relates only to unapproved uses of Evista.”

The case was handled by trial attorneys Jeffrey Steger and Amy Goldfrank of the Justice Department’s Office of Consumer Litigation.

The information is an allegation only. The defendant has agreed to plead guilty to the charge in the information. No finding of guilt is made until the defendant’s plea of guilty is accepted by the court. The complaint for permanent injunction is an allegation only. The defendant has agreed to resolve the complaint for permanent injunction by agreeing to the consent decree of permanent injunction. The consent decree takes effect when signed by the court.

Copies of all of the documents filed with the court today are located at http://www.usdoj.gov/civil/ocl/cases/Lilly/index.htm

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